Comments of Linda Stewart

Comment 1:

In 1997, based on a number of uncertain assumptions, questionable epidemiology and ballpark statistics (from 1995) OEHHA concluded that: "the proportion of all low birthweight newborns in California that may be associated with ETS... corresponds to 1,200 to 2,200 in California in 1995..." and to 9,700 to 18,600 in the nation as a whole (in 1995.)

In 2003, OEHHA now estimates 1,577-1,943 cases of ETS associated low birth weight in California and 24,253- 29,590 in the nation.

These new national numbers (which have seemingly increased by up to 14,000) are based on a single sub-set, (adult females of all ages) from the NHANES (Pirkle) survey of 1995 (published in '96) which was actually conducted between 1988 and 1991, and which attempted to quantify the exposure of nonsmokers to secondhand smoke (Footnote 1, p, ES-11)

But let's note that a similar survey, NHANES 1999 ("Second National Report on Human Exposure to Environmental Chemicals") showed a 75% decrease in serum cotinine levels in American nonsmokers, indicating (if anything) that exposure to ETS had considerably declined since the earlier report.

Response:

Smoking prevalence among pregnant women and in the population in general has indeed decreased since 1985. However, between the first (CDC, 2001) and second (CDC, 2003) National Reports on Human Exposure to Environmental Chemicals, serum cotinine levels have actually risen in parallel with the increase in LBW. In women in the 75th and 90th percentiles, serum cotinine rose 1.49- and 1.85-fold, respectively. Thus a decrease in the median population cotinine level masks increases among women in the upper half of the exposure range. Use of the average cotinine level, reflecting a 75% decrease, is inappropriate because this decrease reflects changes in numbers of persons exposed as well as amount of exposure and does not differentiate between unexposed and exposed. A more appropriate level to use is a level that indicates ETS exposure. That is what was done by OEHHA.

Comment 2:

I therefore find it disturbing that you'd bypass the later study and choose to employ the former, since using the former stats would over-estimate current exposure.

Then too, and just dealing with the national projections, we ought to consider this. (All stats from the CDC.):

UNITED STATES

Year	total % smokers	% pregnant smokers	% LBW of total births
1985	30.2	NA	6.8
1989	[26.8*]	19.5	7.0
1995	24.7	13.9	7.3
1997	24.7	13.2	7.5
2000	23.3	12.2	7.6
2001	22.8	12.0	7.7
2002	[22.5]**	11.4	7.8

* 1989 estimate based on available figures for 1988 (28.1) and 1990 (25.6)
** Average of available figures for 2002.

In other words, while smoking declined 25% and exposure to others' smoke declined 75%, and the number of pregnant smokers declined 40%+ between 1985 and 2002, low birth rates actually rose-- in fact, per the New York Times, to the highest observed levels in the last 30 years. (NY Tlmes, June 26, 2003)

Further, during the period many other suspected risks (teen pregnancy and alcohol consumption by pregnant women) were also in a decline, while preventive measures increased --with record numbers of women getting early pre-natal care. Logically, at least, this should lead to a clear conclusion that the formerly fingered risks, including smoking and ETS, were not as "causative" as was thought. And that productive investigation should begin on another track.

Response:

As mentioned in the response above, smoking prevalence among pregnant women and in the population in general has indeed decreased since 1985. However, between the first (CDC, 2001) and second (CDC, 2003) National Reports on Human Exposure to Environmental Chemicals, serum cotinine levels have actually risen in parallel with the increase in LBW. In women in the 75th and 90th percentiles, serum cotinine rose 1.49- and 1.85-fold, respectively.

Comment 3:

In light of these easily collected statistics, one wonders why OEHHA relied on a single survey of self-reported exposure for women of all ages for 1995 and factored in none of the later relevant clues.

Response:

If the concern is that the updated calculations are inaccurate because they are based on out-of-date data, an alternative calculation of estimated cases for low birth weight due to ETS exposure for the US based on CDC's 2002 National Vital Statistics Report for the year 2000 can be made as follows. In 2000 there were 4,058,814 live births of which 126,241 were multiple, and 3,932,573 were singleton births. Based on the reported numbers of twin (118,916), triplet (6,742), quadruplet (506) and higher order births (77), we estimate that approximately 61,847 women gave multiple births. Thus 3,994,420 women (3,932,573 + 61,847) gave birth in 2000. While there was some variation in active smoking rate with age, the overall smoking rate was 12.2% giving 487,319 smoking, and 3,507,101 nonsmoking mothers. According to the Second National Report on Human Exposure to Environmental Chemicals (CDC, 2003), among nonsmoking women, the serum continine levels for the 75th percentile was 0.179 ng/ml. Thus 25% of nonsmoking women had serum cotinine above this level, indicating exposure to tobacco smoke. Of the nonsmoking mothers, 876,775 (3,507,101 x 0.25) were estimated to be exposed to ETS, which gives an exposure rate of 21.95% (876,775/3,994,420), similar to the 22.7% estimate used above (Pirkle et al., 1996). Thus, use of the 2000 data versus the 1995 data results in similar estimates of exposure and therefore risk. The increased numbers of low birth weight children reflect, in part, population increases.

Comment 4:

Questions arise, too, on the California estimates:

Since 1998, California, in isolation, has virtually ended all exposure to public smoke and boasts of cutting its rates of smoking by incredibly large amounts (about 5%z% below the national average) which would further reduce exposure. Then too, Public Health has so terrified pregnant women on the dangers of ETS, that most women would sooner divorce than let their husbands smoke in the house. Yet the lower range of your estimate has somehow actually climbed (by 377, or 32%)while the upper range has declined by a mere 257. Surely if ETS were a genuine causative factor, your estimate should have declined -- and declined rather drastically-- at both ends of the pole.

So your numbers continue to baffle.

Response:

To clarify a point, in this update we estimated 1,577 excess cases of LBW. The value of 1,943 to which the comment alludes as an upper estimate of LBW is the estimate for pre-term delivery (PTD). The table describing attributable risks was changed during translation into PDF in the Executive Summary and thus in error – the same table in Part B was correct. We apologize for the resulting confusion.

The 1997 OEHHA document used the following equation from the US EPA to calculate the attributable fraction for low birth weight. $a = (1-P_S)(P_E)(R_E-1)/[(1-P_S)(P_E)(R_E-1) + P_S(R_S(P_ER_E+1-P_E))+1]$ *where* P_S *is the prevalence of smoking among pregnant women for which we use the national average of 12.2%.* P_E *is the prevalence of ETS exposure among nonsmokers which is 13.2%.* R_S *is the risk of LBW among smokers for which we use the estimate of 1.58 (Magee et al., 2004).* R_E *is the risk of LBW in ETS-exposed women relative to non-exposed for which we use 1.38. Substituting these values gives an attributable fraction of 4.1% and an estimated 1,347 excess cases of LBW. This calculation explicitly incorporates an estimate of maternal smoking during pregnancy which, unlike most states, California does not collect for its birth data. Use of the national average for prevalence of smoking during pregnancy of 12.2% is probably reasonable. However, if the actual smoking prevalence is lower in California, the number of LBW births attributable to ETS exposure will be higher and closer to the estimate presented in the document.*

Comment 5:

Low Birth Weight: The Epidemiology

Clearly the RRs from your meta-analysis are factored into your Count.

The most notable thing, however, about all the selected studies, both the old and the 7 new, is that what they're all measuring -- each in its own way-- is lower birth weight, as importantly distinguished from Low Birth Weight, officially defined as 5.5 pounds or less.

As OEHHA reported in its first draft revision (6/9/97) the average Lowered Weight among the then-extant studies was a whopping 28 grams (or just shy of a single ounce.)! (p.20) What are we then to determine are the long-term, or even the short-term, health effects of a difference between a baby born at 6 pounds 7 vs 6 pounds 6? And whatever has this to do with Low Birth Weight and all its attendant risks?

Response:

Birth weight is a proxy measure for normal development. In the absence of other disease, decrements in birth weight reflect conditions in utero, from mildly to severely adverse. On a population basis, a decrement of 28 grams may be of little consequence. However, for the individual child this weight decrement may reflect developmental deficits that aren't rectified by the subsequent attainment of normal weight at a later date.

Comment 6:

Apparently not much. Not even among mothers who actively smoke:

> "The deficits of weight at birth of children born to mothers who smoked during pregnancy are overcome by 6 months of age. "
> - Conter et al, BMJ March 25,1995;320

In 1997, I had commented in detail on the underlying studies (seriously flawed) and OEHHA's conclusions (unwarranted, at best) as they appeared in the "final" February draft. I append those comments. And stand by them still.

Yet OEHHA, based only on the first round of studies (whose results it has now--but only now--come to admit "were also consistent with no effect," (p 3-36 of the current draft report) had nonetheless, at the time, made a bold statistical leap to RR 1.4 (a number only attained by omitting the negative findings of the largest summarized study) and concluded (on the gamble its assumptions were all correct) that a body count could be had by playing games with the RR. (6/97)

I continue to find it odd that you were willing to count bodies in 1997 based on studies you now admit were con-sis tent with no effect but which you'd earlier characterized (p 3-35, Feb. '97) as "provid[ing] sufficient evidence that ETS exposure adversely affects fetal growth."

Point: Which is it? Are a series of flawed studies with weak and, even then, non-significant, results; with a lack of controlled confounders; no grip on misclassification; no trending of dose-response, and, yes, as you mention, "wide confidence intervals," whose subject, to begin with, wasn't even Low weight, but merely a missing ounce-- were they actualy "sufficient" to make a leap to an estimate of vast numbers At Risk? Or-- were they not? And if not (as you now suggest) why on earth did you count bodies on the basis of such dross? And why on earth should we trust you now?

Response:

The earlier document (Cal/EPA, 1997) has been subjected to an extensive process of public comment, review by the Scientific Review Panel for Toxic Air Contaminants, and has been

published by the National Cancer Institute as a monograph following their review. The purpose of the current document is to examine more recently published findings which may extend or modify conclusions reached in that document, not to re-open debates which were satisfactorily dealt with in the earlier report. Accordingly, the recently issued call for public comment did not invite comments on the 1997 document, and OEHHA will only respond to those comments which appear to have relevance to the more recent report.

Comment 7:

As for the 7 additional studies, they seem to be no better, at least not statistically speaking, and not enough detail is given to say more. ("Other" isn't enough information about confounders. Nor are we told much about the population of mothers.) And though, seemingly, the studies involved actual Low Birth Weight, as opposed to a missing ounce (?) one wonders about the studies that OEHHA didn't include, and the factors it didn't consider.

For example: After adjusting for active maternal smoking, there are the factors most highly associated with LBW:

Premature delivery:

> "'Ounce for ounce, the babies of smoking mothers had a higher survival rate.' [said Dr. Allen Wilcox, a researcher at the National Institute of Environmental Health Sciences.] Smoking may interfere with weight gain but does not shorten pregnancy. Thus, among smoking women, the smaller babies are more likely to be full term ...[I]t's prematurity not birth weight that explains higher mortality.."
>
> -"High Infant Mortality in US Linked to Premature Births, " Jane Brody, New York Times, March 1, 1995

Low Socioeconomic Class

> "the most powerful single risk factor."
>
> -Redford et al, JAMA June 3, 1998:279.
> Also Olsen et al, Ugeskr Laeger, Sept 19, 1994:156

Race:

> "White infants were heavier and born later than black infants [even though] the white women in this sample smoked more cigarettes"
>
> - Goldenberg et al, Am J Obs & Gyn, Nov., 1996:175
>
> "The rate of Low Birth Weight is twice as high and the rate of Very Low Birth Weight is three times as high for black infants as compared to white infants."

-Luke et al, Int J of Gyn & Obst, March, 1993:40

Poor Nutrition:

"Smoking did not significantly affect infant birth weights." (after adjusting for nutrition.)

-Tchabo, Obst & Gyn, Sept, 1989: 74

"Data suggest that smokers in all social classes have a poorer quality diet."

- Haste et al, Am J Clin. Nutrition, Jan, 1990:51

Occupation:

"A greatly increased risk" for delivering underweight babies was observed among women who worked during their pregnancy. Especially for women required to stand on the job. Job stress, noise and irregular work schedules also increased the risk.

- Am J Obs & Gyn, Sept, 1995.

Other implicated factors:

(Again, after adjusting for active smoking.) Infections. History of induced or spontaneous abortion. First pregnancy after age 30. Medically induced fertilization. Single parenthood. Inadequate weight gain during pregnancy. Chronic illness. Caffeine consumption. Living at a high altitude, and poor dental health.

Response:

As noted in this comment, there are a number of factors that contribute to birth outcomes and perinatal survival. In addition, there is the paradoxical observation mentioned above that "Ounce for ounce, the babies of smoking mothers had a higher survival rate." This seeming paradox is an artifact of the common practice of calculating mortality rates based on the numbers of births occurring at any given gestational age or birth weight. It does not take into account the fact that birth weight is a reflection of the combined effects of fetal growth and the duration of gestation. A recently published analysis resolves this paradox by estimating perinatal mortality rates based on a "fetuses at risk" approach (Joseph et al., 2004) that better reflects the effects of the factors above on fetal and neonatal survival. In this analysis, the number of fetuses at risk of stillbirth at each gestational age were used to calculate gestational age-specific rates of stillbirth. A similar approach was used to calculate gestational age-specific perinatal and neonatal mortality rates.

Application of this technique to live and still births in the U.S. for 1997, stratified by maternal smoking status, showed that growth restriction rates were 1.5-fold higher among smokers than non-smokers at 32-33 weeks of gestation, and approximately 2-fold higher after 34 weeks. Gestational age-specific perinatal mortality rates were also higher among smokers than non-smokers for all gestational ages. In this study there is no evidence that offspring of smokers have a survival advantage at any weight or age. It is reasonable to conclude that the intrauterine environment created in association with maternal active smoke exposure adversely affects fetal growth and survival. Lower birth weight reflects restricted intrauterine growth and/or premature birth, and as such is a proxy measure for increased risk of infant mortality. Indeed, it was associated with increased perinatal mortality among infants of smokers in this study. While this study did not address passive smoking, the association of ETS exposure with lower birth weight and low birth weight is expected to similarly reflect increased risk of mortality.

Joseph, K. S.; Demissie, K.; Platt, R. W.; Ananth, C. V.; McCarthy, B. J., and Kramer, M. S. A parsimonious explanation for intersecting perinatal mortality curves: understanding the effects of race and of maternal smoking. BMC Pregnancy Childbirth. 2004; 4(1):7.

Comment 8:

Surely, not all of these confounders were adjusted for, if indeed such adjustment is actually possible

> "People ... say they'll use statistics to make adjustments for biases and incompleteness. I've spent more than 20 years working as a statistician and I can assure you that you cannot use statistics to adjust."
>
> Dr. Richard Doll, New York Times, Aug 9, 1994

Then, too, since exposure to smoking has gone down, one might as easily postulate, given the economy, that more women are working (and standing on their feet), or more women are under stress. Or can't afford to go to the dentist. Each of these hypotheses is no less of a reach than fingering ETS, and especially in an era when exposure has declined.

Almost needless to say, I find the rest of your figures in the referenced Table to be equally suspect.

Surely you're aware of the unusual method of reckoning that was used by the EPA to arrive at its estimate of 3,000 lung cancer deaths from ETS. A method that included using recently "former" smokers, assumed that any/ ever exposure was a Risk, and was mainly based on questionable epidemiology on the lifelong spouses of smokers.

Now, climbing on top of that, OEHHA appears to estimate that virtually all lung cancer deaths among non-smokers are caused by ETS!? It hardly pays to ask upon what this is based.

So, too, for the climbing levels of heart disease death you now attribute to ETS. In 1994, the Congressional Research Service called the then-current estimate of 37,000 to be, in a word, "implausible." The escalated Number of 69,000+ is, if anything, doubly implausible.

However, you'll get what you're after from this report, --headlines from an ever-credulous media

I understand the futility of attempting to comment, but conscience compels it.

(Low Birth Weight Studies Con't)

I read (in amazement) the first 35 of these incredibly sloppy studies. (P 3-1 to 3-15). The first thing that hit me was the overwhelming waste--waste of money and waste of time --in the hot pursuit of a fictive grail.

All of these studies had disqualifying flaws. Most predominantly: no confounders accounted for. Or big ones not accounted for. (Maternal height and weight; or socio-economics; or working status of mothers--an independent risk, see ** below.) And none appeared to control for such common-sensical factors as the pregnant woman's diet; or alcohol consumption; or vitamin supplementation.... or several other bigs. Confounders that were tested for were usually not listed; nor were numbers frequently given. And a number of other factors were "expected" or "assumed" or "considered to" or "thought to" but not apparently proved.

Then too we get this: very little or no statistical significance and no dose-response (or irrational dose/response), the inclusion of smoking mothers, plus the contradictory data--both between and within--all the individual studies.

Then back to semantics. Negative (or seemingly protective) effects are elaborately rationalized and swept under the rug. (eg, M.acArthur and Knox; Ahlborg and Bodin; Zhang and Ratcliffe) whereas nothing at all's said about the positive (or otherwise inculpatory) anomalies in most of the other studies. And the use of deformed children only may effect the results

Your conclusion thus baffles "All but one of the studies on the impact of ETS exposure in the home... found a decrement in mean birthweight." Underwood et al (0.9 for any paternal smoking), MacArthur and Knox (a 100 gram excess) Yerulshalmy (1.0 among nonsmoking mothers) Mahtai et al ("no difference in the rates of LBW by mother's ETS exposure).

Is that one or is it four? And that's granting all the stuff that's statistically non-significant (which, as it happens here, is most of the stuff you've got.)

Are you daunted? Uh-UH. You conclude (by projection) from egregiously flawed studies which--if accepted, yield statistical "never-mind"-- that the RR attributable to ETS exposure is "1.2 to 1.4" which you then procede to quantify. Endowing us with images of thousands of scrawny babies left bellowing in their cribs.

This is actually shameful.

- "Comment on OEHHA Assessment of ETS," Stewart, April 28, 1997. From original document.

Response:

It is clear that there are a number of confounding factors that influence birth weight. It is also clear from the body of evidence in the epidemiological literature that ETS is one of those factors. The commentator believes the effect of ETS can be explained away but does not provide a clear and compelling argument substantiating the assertion. The implication is that most studies did not account for confounding factors or did not have statistically significant results. While no epidemiological study is perfect, many of the studies did in fact account for specific known confounders. Some of the studies in and of themselves which controlled for confounders were statistically significant (e.g. Jedrychowski and Flak, 1996; Kharrazi et al, 2004, Dejmek et al, 2002). In addition, two meta-analyses provided pooled estimates of decrements in birth weight that were statistically significant (Windham et al., 1999, –24.0 g (95% CI –39.3; -8.6) and Peacock et al., 1998, - 31g (95% CI –44;-19)). Thus, while there are typical problems with some of the epidemiological studies and many show a decrement in birth weight that is not statistically significant, taken together in these two meta-analyses, the studies provide strong evidence of an adverse effect of ETS exposure on birth weight.

References used in responses:

Dejmek, J.; Solansk, y. I; Podrazilova, K., and Sram, R. J. (2002). The exposure of nonsmoking and smoking mothers to environmental tobacco smoke during different gestational phases and fetal growth. Environ Health Perspect. 110(6):601-6.

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Joseph KS, Demissie K, Platt RW, Ananth CV, McCarthy BJ, Kramer MS (2004). A parsimonious explanation for intersecting perinatal mortality curves: understanding the effects of race and of maternal smoking. BMC Pregnancy Childbirth 4(1):7.

Kharrazi M, DeLorenze GN, Kaufman FL, Eskenazi B, Bernert JT, Graham S, et al. (2004). Influence of low level environmental tobacco smoke on pregnancy outcomes. Epidemiol. In press.

Magee, B. D.; Hattis, D., and Kivel, N. M. Role of smoking in low birth weight. J Reprod Med. 2004 Jan; 49(1):23-7.

Peacock JL, Cook DG, Carey IM, Jarvis MJ, Bryant AE, Anderson HR, et al. (1998). Maternal cotinine level during pregnancy and birthweight for gestational age. Int J Epidemiol 27(4):647-56.0300-5771

Windham GC, Eaton A, Hopkins B (1999). Evidence for an association between environmental tobacco smoke exposure and birthweight: a meta-analysis and new data. Paediatr Perinat Epidemiol 13(1):35-57.